REMARKS

Claims 1-3, 7-12, and 14-24 are pending in this application. Non-elected claim 12 has been withdrawn from consideration by the Examiner. By this Amendment, claims 1-3, 10, and 15 are amended; claims 4 and 5 are canceled; and claims 21-24 are added. Support for the amendments to the claims and new claims may be found, for example, in the originally filed claims and in the specification at p. 5, ll. 7-9; p. 6, ll. 12-28; and pp. 8-12. No new matter is added.

In view of the foregoing amendments and following remarks, Applicants respectfully request reconsideration and allowance.

I. 35 U.S.C. §112, Second Paragraph Rejection

Applicants thank the Examiner for withdrawing the previously asserted 35 U.S.C. §112, second paragraph rejection.

II. Claim Objection

The Office Action objects to claim 10 for informalities. By this Amendment, claim 10 is amended according to the Examiner's helpful suggestion. Accordingly, Applicants respectfully request reconsideration and withdrawal of the objections.

III. 35 U.S.C. §112, First Paragraph Rejection

The Office Action rejects claims 1-5, 7-11, and 14-20 under 35 U.S.C. §112, first paragraph. Applicants respectfully traverse the rejection for at least the following reasons.

Without conceding the propriety of the rejection, claim 1 is amended to recite components of the aqueous and oil phases and to recite non-ionic emulsifiers. These various features are described in the specification and are enabled therein. Thus, one of skill in the art would be enabled by the specification to practice the claimed invention.

Accordingly, Applicants respectfully request reconsideration and withdrawal of the rejections.

IV. 35 U.S.C. §103(a) Rejection

A. Higashi, Joscelyne, Moeritz, and Forster

The Office Action rejects claims 1-5, 7-10, and 14-17 under 35 U.S.C. §103(a) over Higashi et al., *Size of lipid microdroplets effects results of hepatic arterial chemotherapy with an anticancer agent in water-in-oil-in-water emulsion to hepatocellular carcinoma*, 289 J. Pharmacology and Experimental Therapeutics 816-819, no.2 (1999) ("Higashi") in view of Joscelyne et al., *Membrane emulsification-a literature review*, 169 J. Membrane Sci. 107-117 (2000) ("Joscelyne"), DE 19630176 to Moeritz ("Moeritz"), and Forster et al., *Production of fine disperse and long-term stable oil-in-water emulsion by the phase inversion temperature method*, 13 J. Dispersion Sci. and Tech. 183-193, no.2 (1992) ("Forster"). As to the remaining claims, Applicants respectfully traverse the rejection.

The combination of Higashi, Joscelyne, Moeritz, and Forster would not have rendered obvious the process of claim 1 for at least the following reasons.

1. Failure To Establish That The Temperature Claimed In B) Is A Result-Effective Variable

The combination of Higashi, Joscelyne, and Moeritz does not teach or suggest a process as recited in claim 1, including step b), which recites: "emulsifying the aqueous phase by passing the aqueous phase through a largepored, porous membrane into an oil phase, wherein the aqueous and oil phases are heated to a temperature of from 30°C to 35°C before said emulsification."

As discussed in the previous response, the Office Action acknowledges that Higashi, Joscelyne, and Moeritz fail to teach this feature, but asserts that it would have been obvious to optimize the temperature conditions because temperature is allegedly a result-effective variable. However, this mere assertion is insufficient to support a *prima facie* case of obviousness.

The Examiner attempts to support this assertion by pointing to Joscelyne's teachings, namely that "temperature can be an important parameter in emulsification affecting both the viscosity of the dispersed and continuous phases and also the nature of the emulsifier as a consequence of phase inversion temperature." *See* Office Action at page 5. The Office Action also asserts Joscelyne's teachings that "emulsification temperature usually dictated by the requirements of a product."

Applicants address these assertions in turn. First, the mere fact that something "can" be an important parameter does not make that parameter a result-effective variable. Second, the mere fact that a parameter is "usually" dictated by the requirements of a product also does not make parameter a result-effective variable. For optimization to be obvious, a variable must be recognized in the art as a result-effective variable. The asserted teachings do nothing more that set forth possibilities. The fact that something "can" be important does not mean it "is" important, and the fact that something is "usually" dictated by a product, does not mean it always is dictated by such.

Indeed, Joscelyne clearly states that "<u>there have been no systematic studies of the effects of temperature on membrane emulsification</u>" (emphasis added). *See* Joscelyne at section 3.5. From this teaching, one of skill in the art would not have had a reason to optimize the temperature in <u>membrane emulsification processes</u> with any reasonable expectation of predictable results. Indeed, one of skill in the art would not know in which direction and under

what rules he/she would have to establish his experiments, particularly in view of the fact that the references fail to provide teachings on how temperature itself might influence membrane emulsification.

As such, the Office Action fails to establish that the temperature is a result-effective variable and that the claimed range of "30°C to 35°C" would have been *prima facie* obvious in view of the applied references.

2. Failure To Teach Or Suggest C)

The combination of Higashi, Joscelyn, and Moeritz also fails to teach or suggest "c) phase inversion of the heated emulsion from b), by cooling the mixture at a cooling rate of at least 0.3 K/min, where a non-ionic emulsifier is added to the oil phase in b)" as recited in claim 1 for at least the following reasons.

a. Failure To Establish That The Cooling Rate Is A Result-Effective Variable

The Office Action acknowledges that Higashi and Joscelyne do not teach "phase inversion of the heated emulsion from b), by cooling" as claimed. However, it asserts that in view of Moeritz and as evidenced by the Encyclopedia of Pharmaceutical Technology ("Encyclopedia"), that the cooling rate is a result-effective variable.[1] The Office Action references the Encyclopedia to allegedly support its assertion that cooling rate is a result-effective variable. Applicants first note that this reference was published in 2007, years after the November 5, 2003 priority date for the instant application. As such, the Office Action's blanket

[1] If the rejection is maintained, Applicants request that the role of the Encyclopedia be clarified, because it is not listed as part of the reference combination on page 4.

assertion that Moritz and the Encyclopedia establish that cooling rates are result-effective variables is insufficient, particularly as evidence for what one of skill in the art would have considered to be a result-effective variable in 2003. Moreover, the Office Action fails to set forth any evidence or reasoning that would establish that a cooling rate is always a result-effective variable and therefore obvious to optimize/modify.

The Office Action continues to assert Forster, but in view of the Office Action's updated position using the Encyclopedia, it is unclear how or why Forster is asserted. In any event, Forster fails to establish that the cooling rate is a result-effective variable or that it would have been obvious to optimize it. Forster does not, nor is it asserted to, teach or suggest the specific cooling rate. However, it has been relied on to support the Office Action's assertion that it would have been obvious for one of ordinary skill in the art to optimize the cooling rate in view of Forster because in Forster the cooling rate was allegedly insignificant. The fact that the cooling rate in Forster was insignificant has nothing to do with the cooling rate in the process of claim 1. Forster does not teach or suggest, alone or in combination with the other references, how to produce w/o/w emulsions as claimed. The process of Forster is not the same as or even similar to claim 1, and as such, one of ordinary skill in the art would not have modified the already deficient reference combination in view of Forster to yield the claimed process.

A *prima facie* case of obviousness has not been established with respect to this feature, and as such, the rejection is improper.

b. Moeritz's Failures

Despite the submission of the translated Moeritz, the Office Action still maintains it rejection, which depends on the combination of Moeritz with the other applied references. In view of the clear differences between the Moeritz process and that of claim 1, Applicants

respectfully submit that the Office Action has not established a reason to combine Moeritz with the other applied references, let a *prima facie* case of obviousness. Indeed, the Office Action fails to address the reasons previously presented by the Applicants that discredit the combination of Moeritz with the other references. In particular, Moeritz does not teach or suggest a process with one aqueous phase. As such, the picking and choosing of Moeritz's process limitations would not have been obvious to one of skill in the art where the process is for a W/O/W emulsion with "an aqueous phase."

Furthermore, as described in the previous response, the phase inversion process described in Moeritz is substantially different from that of claim 1. Moeritz discloses the principle method of transferring an o/w emulsion to a w/o emulsion, and vice versa. *See* Moeritz Translation (previously provided) at p. 4, lns. 13-21. Moeritz does not, however, disclose a "process for the preparation of … multiple emulsions of water/oil/water (W/O/W) type" that are produced via "phase inversion" as recited in claim 1. The process of claim 1 results in a w/o/w type emulsion where "the aqueous phase" that contains the active ingredient is found on the outer and inner water phases. Instead, the process of Moeritz is designed to integrate THREE distinct solutions (A, B, and C). In particular, because the outer and inner water phases in Moeritz have distinct compositions, the outer water-phase is not produced from the prior water phase of the w/o emulsion as is the case in instant claim 1. For at least this reason, there is no reason provided by Moeritz to modify the other references as claimed and the combination of applied references would not have rendered obvious claim 1. As such, at least Moeritz's combination with the other references is unsupported by a sufficient rationale for making the combination in the first place and, thus, a *prima facie* case of obviousness has not been set forth.

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Claim 1 would not have been rendered obvious by the combination of Higashi, Joscelyne, Moeritz, and Forster. Claims 2, 3, 7-10, and 14-17 depend from claim 1 and, thus, also would not have been rendered obvious by the applied references. Accordingly, Applicants respectfully request reconsideration and withdrawal of the rejection.

B. Higashi, Joscelyne, Moeritz, Forster, and Ganne

The Office Action rejects claims 1, 10-11, and 18-20 under 35 U.S.C. §103(a) over Higashi, Joscelyne, Moeritz, Forster, and U.S. Patent No. 6,251,407 to Ganne et al. ("Ganne"). Applicants respectfully traverse the rejection.

The deficiencies of Higashi, Joscelyne, Moeritz, and Forster with respect to claim 1 are described above. Ganne, which is only relied upon by the Office Action for its alleged disclosure of the additional limitations recited in claims 11 and 18-20, at least fails to cure the deficiencies of the combination of Higashi, Joscelyne, Moeritz, and Forster with respect to claim 1. As such, the combination of Higashi, Joscelyne, Moeritz, Forster, and Ganne fails to teach or suggest each and every limitation of claim 1 and its dependent claims.

In addition to the above reasons, claims 11 and 18-20 would not have been obvious for the following additional reasons. The Office Action acknowledges that Higashi, Joscelyne, Moeritz, and Forster do not teach an active ingredient that is encompassed by claims 11 and 18-20. Ganne does not cure this deficiency. Although Ganne discloses some emulsions that may be prepared according to conventional methods, Ganne fails to describe the process according to claim 1. One of ordinary skill in the art would therefore have had no reason to assume in view of Ganne, that the specific parameters and steps outlined in claim 1 would be applicable to the compositions described in Ganne. The Office Action asserts that substitution of one active ingredient for another would have been obvious. However, there is no suggestion or teaching to

use the actives in Ganne in the process as claimed – especially since Ganne describes a totally different process. Substitution of the active ingredients in different processes would not have been obvious. As such, a *prima facie* case of obviousness has not been established with respect to claims 11 and 18-20.

Accordingly, Applicants respectfully request reconsideration and withdrawal of the rejection.

IV. Rejoinder

Applicants also respectfully request rejoinder of non-elected claim 12. This application is subject to unity of invention practice as set forth in PCT Rule 13. *See* MPEP §1893.03(d). There is no lack of unity of invention between claim 1 and withdrawn claim 12. In fact, claim 12 depends from claim 1 and, thus includes all the limitations of claim 1. For at least the reasons presented above, claim 1 is believed to be patentable. Accordingly, dependent claim 12 is also believed to be patentable. Applicants respectfully request withdrawal of the Restriction Requirement and rejoinder of claim 12.

V. New Claims

By this Amendment, new claims 21-24 are presented. New claims 21-24 depend from claim 1 and, thus, distinguish over the applied references for at least the reasons discussed above with respect to claim 1. Prompt examination and allowance of new claims 21-24 are respectfully requested.

VI. Conclusion

In view of the foregoing, Applicants respectfully submit that this application is in condition for allowance. Applicants earnestly solicit favorable reconsideration and prompt allowance of the application.

Should the Examiner believe that anything further would be desirable to place this application in even better condition for allowance, the Examiner is invited to contact the undersigned at the telephone number set forth below. Applicants authorize the Commissioner to charge Deposit Account No. 50-4254, referencing Attorney Docket No. 2901652-000004 for fees due or any deficiencies of fees and to credit any overpayments.

Respectfully submitted,

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November 9, 2010

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